

Fig. 1

1 CAGCTCTCAT TTCTCCAAA ATGTGTTTGA GCCACTTGGA AATATAGCCT TTAAGCCATT CAAGAACTCA AGGAGCTCAG AGATCATCCT GGAAGCTGTG
 CTCGAGAGTA AAGAGGTTTT TACACAACCT CGGTGAACCT TTTATACGGA AATTGCGTAA GTTCTTGAGT TCCTGAGATC TCTAGTAGGA CCTTGACAC
 1 MetCysLeus erHisLeuGI uAsnMetPro LeuserHis exArgThrGI nGlyAlaGI nArgserSer rPlySLeuTrp

101 GCTCTTTTGC TCAATAGTTA TGTGCTATT TCTTGTCTCC TTCAGTTGGC TAATCTTTAT TTTTCTCCAA TTAGAGACTG CTAAGGAGCC CTGTATGGCT
 CGAGAAAACG AGTTATCAAT ACAACGATAA AGAAAACGAG AAGTCAACCG ATTAGAATA AAAAGAGGT AATCTCTGAC GATTCTCTCG GACATACCGA
 28 LeupheCys SerileValM etLeuLeupH eleuCysser PheserTrpL euilePheIl ePheLeuGI nLeuGIuThra lAlysGIuPr ocysMetaIa

201 AAGTTTGAC CATTACCCTC AAAATGGCAA ATGGCATCTT CTGAACCTCC TTGGGTGAAT AAGGTGTCTG ACTGGAAGCT GGAGATACTT CAGAATGGCT
 TTCACAACCTG GTAATGGAG TTTTACCCTT TACCCTAGAA GACTTGGAGG AACGCACTTA TTCCACAGAC TGACCTTCGA CCTCTATGAA GTCTTACCGA
 LyspheGlyP roleuProse rLysTrpGI nMetaIasers erGIuProPr ocysValasn LysValsera sPTripLysle uGIuileLeu GIasnGlyLeu

301 TATATTTTAT TTATGGCCAA GTGGCTCCCA ATGCAAACTA CAATGATGTA GCTCCTTTTG AGTGCGGCT GTATAAAAAC AAAGACATGA TACAACCTCT
 ATATAAATTA AATACCGGT CACCGAGGGT TACGTTTGA TTTACTACAT CGAGGAAAAC TCCACGCCGA CATATTTTGG TTCTGTACT ATGTTTGAGA
 95 TyrLeuIl eTyrGIyGI nValAlaProa snAlaAsnTy rAsnAspVal AlaProPheG luValArgle uTyrLysAsn LysAspMetI legInThrLeu

401 AACAAACAAA TCTAAATCC AAAATGTAGG AGGACTTAA CAATTGCATG TTGGGGACAC CATAGACTTG ATATTTCACT CTGAGCATCA GCTTCTAAA
 TTGTGTGT TTAGTTTAGG TTTTACATCC TCCCTGAATA CTTAACGTAC AACCCCTGTG GTATCTGAAC TATAAGTTGA GACTCGTAGT CCAAGATTTT
 128 ThrAsnLys SerLysileG lAsnValGI yGIyThrTyI GlueuHisv aGIyAspTh rIleAspLeu IlePheAsns erGIuHisGI nValLeuLys

501 AAIVAAVACAV ACTGGGGTAT CATTTTACTA GCAATCCCTC AATTCAVCTC CTAGAGACTT GATTGTGAVCT CCTCAVTTCC TTACAGACAT GTAGAGGTGC
 TTTATATGTA TGACCCCATTA GTAATAATGAT CGTTTAGGGG TTAAGTTAGAG GATCTCTGAA CTAAACTAGA GGAGTAAGGG AAGTGTGTA CATCTCCACG
 161 AsnAsnThrT yTrpGIyI lIleLeuLeu AlaAsnProG lnpheIlese rAm*

601 CAGTGGGTGG ATTGGAGGGA GAAGATATTC AATTCTCTAGA GTTGTCTGT CTACAAAAT CAACACAAC AGAACTCCTC TGCAAGTGAA TTTTCATCTA
 GTCAACCCACC TAACCTCCCT CTCTATAAG TTAAGATCT CAACACAGACA GATGTTTTTA GTTGTGTG TCTTGAGAGG ACGTGCACTT AAAAGTAGAT

701 TCATGCCCTAT CTGAAGAAGA CTCAGGGGAA GAGCCAAAGA CTTTGTGTG GATCTGCAGA AATACTTCAT TAATCCATGA TAAACAACAAT ATGATGACA
 GTACGGATA GACTTCTCT GAGTCCCTCT CTGGGTTTCT GA AAAACCAAC CTAGACGTCT TTATGAAGTA ATTAGGTACT ATTTGTTTTA TACCTACTGT

801 GAGGACATGT GCTTTTCAAA GAATCTTTAT CTAATCTCTG AATTCATGAG TGA AAAAATG GAGTCTTAT CCCATGGAAG AATTACCTGG TATGCAAAAA
 CTCCTGTACA CGAAAAGTTT CTTAGAATA GATTAAGAAC TTAAGTACTC ACCTTTTTAC CTCAAGATAA GGGTACCTTC TAAATGAGAC ATACGTTTTT

901 GGATCTGGGG CAGTAGCCTG GCTTGTCTCT CATATCTCTG GCCTGCTGTA ATTCACTCT CTCTACTCC CATCTTCTGA GACCTCCCA ATAAAAAGTA
 CCTAGACCCC GTCATCGGAC CGAAAACAAGA GTATTAAGAAC CCGACGACAT TAAGTAAGAA GAGTATGAGG GTAGAAGACT CTGGGAGGGT TATTTTTCAT

1001 GACTGATAGG ATGGCCACAG ATATGCCCTAC CATACCCTAC TTTAGATATG GTGTGTGTAG AAGATAAAGA ACAATCTGAG AACTATTGGA ATAGAGGTAC
 CTGACVATCC TACCGGTCTC TATACGATG GTATGGGATG AATCTATAC CACCACAATC TTCTVATCTC TCTVATGACTC TTGATTAACCT TATCTCCATG

1101 AAGTGGCATA AAATGAATG TACGCTATCT GGAATTTCT CTGTGTTTTA TCTTCTCTAG GATGACAGGT GCTTTAAAAA GCCTTATCAA AGGAGTCATT
 TTCACCCCTAT TTTACCTTAC ATGCGATPAG CCTTTAAGA GAACCAAAAT AGAAGAGTCT CTACGTCCCA CGAAAVTTTTT CGGAATAGTT TCCCTCAGTAA

1201 CGGAACCCCTC ACGTAGAGCT TTGTGAGACC TTACTGTGTC TGCTGTGTCT TAAACATTCG TAATTCVAAA GAAAGAGTAA CCATTAGTAA TCAATTAGGTT
 GGCTTGGGAG TGCATCTCGA AACACTCTGG AATGACAACCT AATGACAACCT AATGACAACCT AATGACAACCT AATGACAACCT AATGACAACCT AATGACAACCT

1301 TAACCCAGCA ATGTAATTAT CATTAATGCA TTAATGCAATG TTAATGATTTA GAAATTTTATG CTAGCTTTCC AGATTTGCA AAGTGCCTTC GTAACAGT
ATTGGGCTCT TACCAATAATA GAAATGACCT AATACAGTAC ATTACTTAAT CATTAATAATC GATCGAAGG TGTCAAAAGT TTCAAGAAAG CATTTTGTCA
1401 TAGCAATTCCT ATGAAGTTAA TTGGGCAAGC AATTTGGGGA AAATTTTATG GATGAGATG TGAATAGCATA GCATAGCCAA CTTTCCCTCA CTCATAGGAC
ATCGTTAAGA TACTTCAATT AACCCGTCCG TAAACCCCTT TTTAATAATCA CTACTCTTAC ACTATCGTAT CGTATCGGTT GAAAGGAGTT GAGTATCTG
1501 AAGTGAATAC AAGAGCAAT GGTAGTCCC CTGATTTGCA CTGTCTCAGC TTTAGAATG TTAATTTCTGC TATCGTTTA TAAGACTCTA AAACCTTAGC
TTCACGTGATG TTCTCCGTTA CCCATCAGG GACGTAACTG GACAGAGTGC AAATCTTAAC AATAAGACG ATAGCAAT ATTCTGAGAT TTGAATCCG
1601 AATTCACTTT TCAGGAAGCA TATTCCTCTT TAGCCCAAGG TGAGCAGAGT GAAGCTTTC CATTAACAGC ACACTTTTCT TTTTCTTCC
TTAGTGAAA AGTCCCTTCT ATAAGGGAA ATCGGTTCC ACTGCTCTCA CTTCGATGTT GTCTAGAAAG GAAATGCTG TGTGAAAAA AAAAAAAG
1701 TGCCGTAATC AGGAGATCC AGGATGCTGT TCAGGCCAAA TCCCAACCAA ATTCCTTTGCA GGGCCCATCT TAGTCAATG TGCTTACTTC
ACGACTTAG TCCCTCTAGG TCCCTACGACA AGTCCGCTTT AGGCTTGCTT TAAAGGAAA AGTGAACGT CCCGGGTAGA ATCAGTTTAC ACGATTGAAG
1801 TAAATATAATA AATAGCACA ATTCAAAAT TTTGGAATCT TAAATTAGCT ACTTGCTGGA AAGNATATA ATGATTACAT TGTAAACAAA
ATTTTATTAT TTATCGTGAT TAACTTTTAA AAACCTTAGA ATTTAATCGA TGAACGNCA ACGAACAACT TTCCNTATAT TACTAATGTA ACATTTGTTT
1901 TTTTAAATAT TTATGATAT TTGTGAAG CTTGATTAATG TTAATAATA TTAATGTAAG AGCT
AAATTTTATA AATACCTATA AACACTTTTC GACGTAATAC AATTATATAT AATGATACAT TCGA

Fig. 1 (cont.)

			<u>A</u>			<u>A'</u>	<u>B'</u>
DNA 19355	52	ETAKEPCMAKFG	-----	PLPSK	---	WQMASSEP	PCVNKVSDWK--
TNF- α	84	PSDK-PVAHVVA	-----	NPQAEQ	QLQ---	WLNRR	ANALLANGVELRDNQ
Apo2L	119	GPQR-VAAHITGTRGRSNTLSSPNSKNEKALGRKINSWESSRSGHSFSLNLH	---	LRNGE			
CD95L	142	E-LR-KVAHLTG	-----	KSNSRSM	PLE---	WEDTY	GIVLLS-GVKYKKG
LT α	59	STLK-PAAHLIG	-----	DPSKQN	SLL---	WRANT	DRAFLQDGFSLSNNS
		<u>B</u>	<u>C</u>		<u>D</u>		<u>E</u>
DNA 19355	86	LEILQNGLYLIYQVAPNAN	-----	YNDVAPFEVRLYKNK	---	DMIQTLTNK	SKIQN
TNF- α	124	LVVPSEGLYLIYSQVLFKGQGCP	---	STHVLLTHTISRIAVS	---	YQTKVNLLSAIKS	
Apo2L	175	LVIHEKGFYIYSQTYFRFQEEIKENTKNDKQMVQYIYKYTSYDPPI	---	LLMKSARNSC			
CD95L	182	LVINETGLYFVYSKVYFRGQSC	-----	NNLPLSHKVYMRNSKY	---	PQDLVMEGKMMS	
LT α	99	LLVPTSGIYFVYSQVVFSGKAYSPKATSSPLYLAHEVQLFSSQYPFHVPLL	---	SSQKMVY			
			<u>F</u>		<u>G</u>		<u>H</u>
DNA 19355	136	-----	VGGTYELHVGD	TIDLIFNSEHQVLKNNT	---	YWGIIILLANPQF	IS
TNF- α	176	PCQRETPEGAEAKPWYEPIYLGGVFQLEKGDRLSAEINRPDYLDFAESGQVYFGI	---	IAL			
Apo2L	232	-----	WSKDAEYGLYSIQCGIFELKENDRIFVSVTNEHLIDMDHEA	---	SFFGAF	LVG	
CD95L	233	-----	YCTTGQMWARSSYLGA	VFNLT	SADHLYVNVSELSLVNF	---	EESQTFFGLYKL
LT α	157	-----	PGLQEPWLHSMYHGAA	FQLTQGDQLSTHTDG	IPHLVL	---	SPSTVFFGAFAL

Fig. 2

Fetal
Human

Human 1
Adult

Human 2
Adult

Cancer

FB
-9.3
-7.3
-4.4
-2.4
-1.35

Kidney
Liver
Lung
Brain

Pancreas
Kidney
Sk. muscle
Liver
lung
Placenta
Brain
Heart

PBL
COLON
SM. INTEST
OVARY
Testis
prostate
Thymus
Spleen

G-361
A549
SW480
Raji
MOLT-4
K-562
Hela S3
HL60

Fig. 3

09495368 111898

09496356-11493

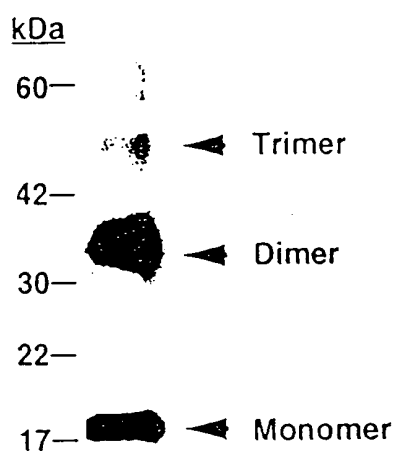


Fig. 4

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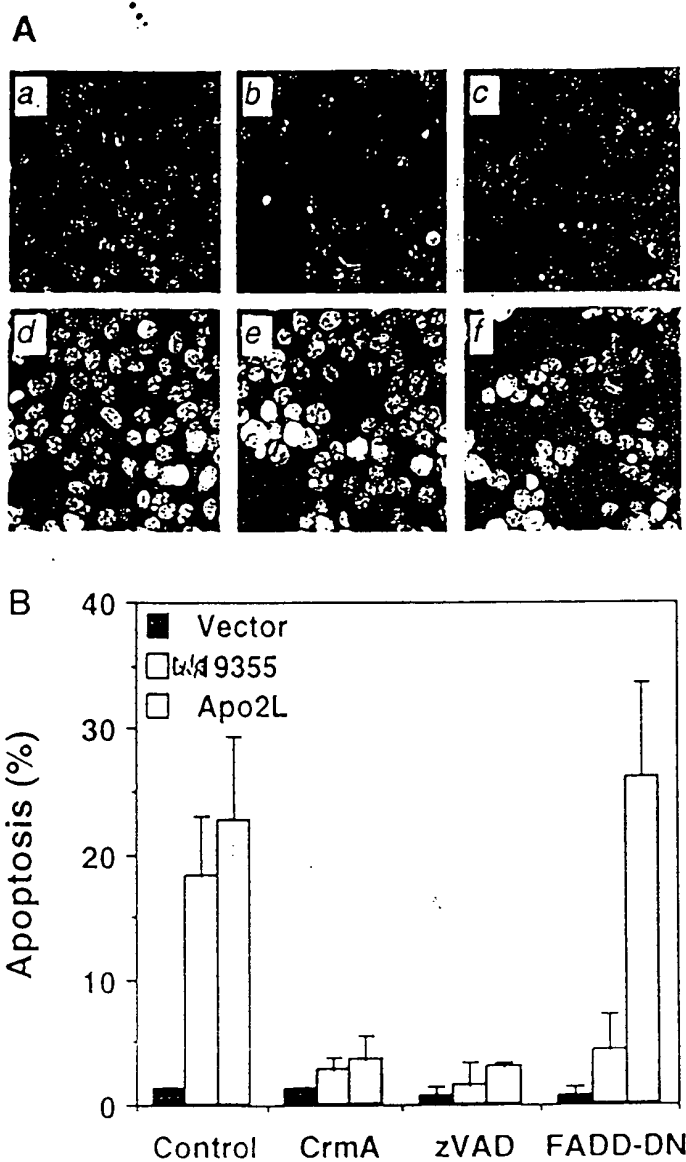


Fig. 5

363T 8936T60

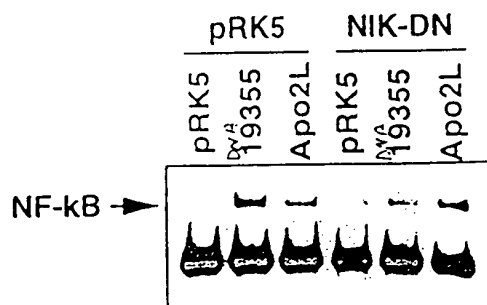


Fig. 6

hG ITR 1 MAQHGA **MGAF** **FRA** **LCGL** **LAL** **LCAL** **SL** **GORP** - TGG **PGCG** **PG** **RLL** **LTG** **TDA** **RC** CRD1
 mG ITR 1 - - - - - **MGAW** **AML** **YQV** **SML** **CVLD** **LGA** **PSV** **VEE** **PGCG** **PG** **KVQ** **NGS** **G** **NNT** **RC** CRD2
 hG ITR 50 **CRVHTTRCCRDY** **PGEE** **CC** **SEWD** **CMCV** **OPE** **FHCG** **DP** **CCT** **TCRH** **HP** **PP** **PGQG**
 mG ITR 45 **CSLYA** - - - - - **PGKE** **DC** **PKERC** **ICVT** **PEYH** **CGDP** **QCK** **ICK** **HY** **PC** **Q** **PGQR**
 hG ITR 100 **VQSQG** **KFS** **PGF** **QC** **IDCAS** **GTFS** **GGHE** **GHCK** **PWTD** **CT** **QFG** **FLT** **V** **EPGN** **KTH** CRD3
 mG ITR 88 **VESQG** **DIV** **FGFR** **CVAC** **AM** **GTFS** **AGRD** **GHCR** **LWTN** **CS** **QFG** **FLT** **M** **EPGN** **KTH**
 hG ITR 150 **NAVC** **V** **PGSP** **PA** **EPL** **GWLT** **VVL** **LAV** **AAC** **VLL** **LTSA** **QLGL** **HWQL** **RS** **QCM** **WP** TM
 mG ITR 138 **NAVC** **I** **PEPL** **PT** **EQY** **GHL** **TV** **IF** **LV** **MAAC** **IFF** **LT** **TV** **QLGL** **HWQL** **R** **QH** **M** **C** **P**
 hG ITR 200 **RETQ** **LLL** **EV** **PP** **ST** **EDAR** **SC** **FP** **EE** **ER** **GER** **SA** **EEK** **GR** **LD** **LWV**
 mG ITR 188 **RETQ** **PFA** **EV** **QL** **SA** **EDAC** **S** **FP** **EE** **ER** **GE** **Q** - **T** **EEK** **CH** **L** **G** **GR** **WP**

Fig. 7

00105369-44098

CD95-Ig
DR4-Ig
DR5-Ig
TNFR1-Ig
TNFR2-Ig
Apo3-Ig
h-GITR-Ig
Control

22 Kda
17 Kda

Fig. 8

B

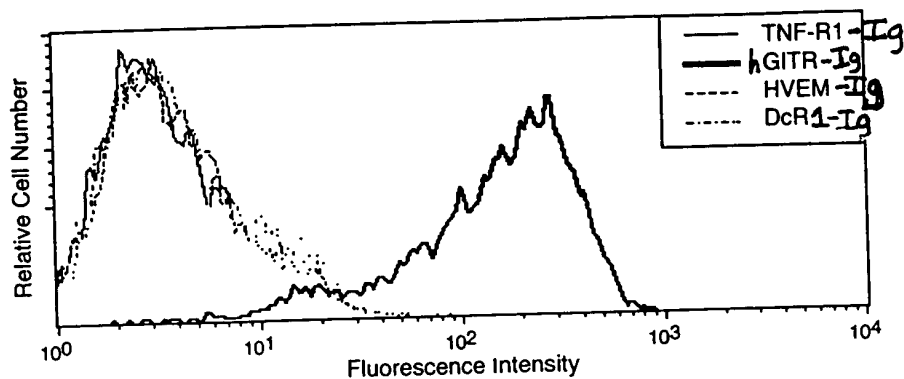


Fig. 9A

C

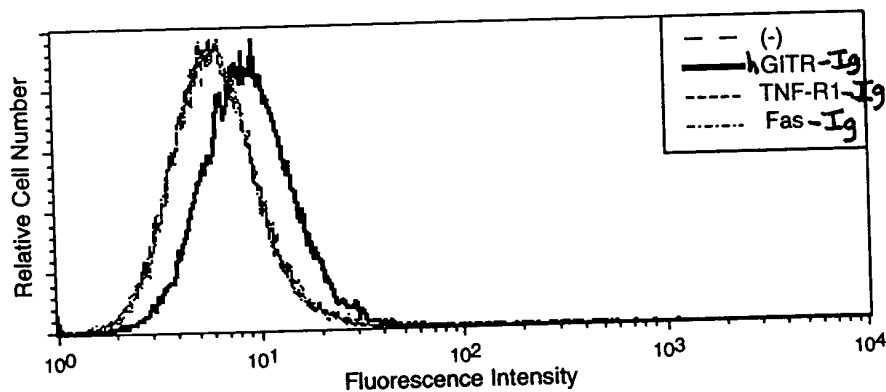


Fig. 9B

36811-9956T60

Transfected	Expression Vector	Relative Luciferase
-	-	~1.0
-	+	~1.0
+	-	~4.5
+	+	~26.0

hGTR
DNA 19355

Fig. 10

A bar graph showing Relative TNF levels on the y-axis (0 to 25) for two cell types, Tcell and Macrophage, under two conditions: + buffer and + DNA 19355. The Tcell + DNA 19355 condition shows a significantly higher relative TNF level (approximately 21) compared to the other three conditions, which are all below 2. Error bars are present for each bar.

Cell Type	Condition	Relative TNF level (approx.)
Tcell	+ buffer	1.0
	+ DNA 19355	21.0
Macrophage	+ buffer	0.8
	+ DNA 19355	1.5

Fig. 11